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EXAMINER	
MCGARRY, SEAN	
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1635	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/552,914	CLAWSON ET AL.	
	Examiner	Art Unit	
	Sean R. McGarry	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *160-174* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *160-174* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/05/09 has been entered.

The declarations filed 5/5/09 and the evidence filed therewith are of sufficient weight to remove the Taira [2004/002077] reference of record as prior art.

A new ground of rejection is set forth below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 160-174 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nilsen et al [US 6,013,447] in view of Tuschl et al [2004/0259247], Li et al [US 2002/0114784], Turner et al [US 2004/0053876]. Paddison et al [Genes & Development Vol. 16:948-958, 2002], Brummelkamp et al [Science, New Series Vol. 296(5567):550-5534/19/2002], and Hertzel et al [Journal of Lipid Research, Vol. 41: 1082-1086, 2000].

The invention is as clearly set forth in the claims.

Nilsen et al have taught a vectors and methods of their use in identifying affector RNA molecules (see Figure 1, for example). The vectors are taught to contain a "targeting gene" which encodes an affector RNA which is "an RNA molecule that is designed to alter, or preferably inhibit, the expression of an RNA of interest" where "preferred affector RNA molecules are ribozymes, external guide sequences, antisense RNA, and triple helix-forming RNA" (see columns 8-9, for example). These affector molecules are targeted to a fusion transcript that encodes a target nucleic acid molecule fused to a reporter molecule that can be directly or indirectly detected including a fluorescent polypeptide fusion (see columns 6-7, for example). Nilsen et al have taught a vector construct as recited for use in the instantly claimed method where the vector of

Nilsen is used to identify affector RNA molecules. Nilsen et al does not explicitly direct one to use weak promoters, but indicates at column 8, lines 5-10, that any suitable promoter can be used. At column 8, lines 39-49, various preferred promoters are suggested and includes the HSV thymidine kinase promoter which is known in the art as a weak promoter. The difference between the prior art and the instant invention is the recitation of an RNA affector that induces RNA interference. RNA interference was not known at the time of Nilsen et al invention, but would be RNA affectors since they are RNA oligomers that inhibit a target nucleic acid such as an mRNA. The prior art does indeed provide a description of such affectors expressed from a vector as required by the instant claims.

Tuschl et al disclose that siRNA compounds can be expressed from vectors for the inhibition of a desired target, see paragraph [0035], for example. I et al have also taught the use of vectors for the expression of RNA interfering nucleic acids, see paragraphs [0036] and [0045][-[0046], for example.

Turner et al have also taught the expression of RNA interfering agents utilizing various promoters, including U6 promoters, for example. Turner et al have also taught the following:

[0008] Therefore, the present invention provides a composition comprising a hairpin siRNA molecule, wherein the molecule comprises three contiguous regions, a first region, a second region, and a third region, where at least a portion of the first region is substantially complementary to and pairs to at least a portion of the third region forming a duplex comprising about 18-29 nucleotides in length, wherein either the first region or the third region is complementary to a target RNA, and wherein at least a portion of the second region is complementary to the target RNA. In some embodiments, the RNA duplex is about 19-23 nucleotides long; in other embodiments, the RNA duplex is about 19 nucleotides long. In some embodiments, the second region is at least 3 nucleotides long; in other embodiments, the second

region comprises from 3 to 7 nucleotides; in other embodiments, the second region comprises 3 to 4 nucleotides.

[0009] In other embodiments, the present invention provides a composition comprising a hairpin siRNA molecule wherein the molecule comprises three contiguous regions, a first region, a second region, and a third region, where at least a portion of the first region is substantially complementary to and pairs to at least a portion of the third region forming a duplex comprising about 18-29 nucleotides long, wherein either the first region or the third region is complementary to a target RNA, wherein either portion of the first region or the third region in the duplex comprises at least one mismatch. In some embodiments, the first region is complementary to a target RNA, and the third region comprises at least one mismatch. In other embodiments, the third region is complementary to a target RNA, and the first region comprises at least one mismatch. In other embodiments, at least a portion of the second region is complementary to the target RNA. In some embodiments, the RNA duplex is about 19-23 nucleotides long; in other embodiments, the RNA duplex is about 19 nucleotides long. In some embodiments, the second region is at least 3 nucleotides long; in other embodiments, the second region comprises from 3 to 7 nucleotides; in other embodiments, the second region comprises 3 to 4 nucleotides.

[0010] The present invention also provides a composition comprising a multiplex siRNA molecule, wherein the multiplex siRNA comprises at least two siRNA molecules connected by a linker. In some embodiments, at least one of the siRNAs is a hairpin siRNA, as described in any of the embodiments above. In other embodiments, the multiplex siRNA comprises at least two hairpin siRNA molecules connected by a linker; in further embodiments, the linker is a linking sequence. In further embodiments, at least one linking sequence comprises a processing site. In yet further embodiments, the processing site is a cleavage site.

[0011] The present invention also provides a composition comprising a DNA molecule encoding at least one strand of a siRNA molecule. In some embodiments, the strand is a single strand of a double stranded siRNA molecule, where at least one strand of the double-stranded siRNA is complementary to a target RNA. In other embodiments, the strand is a hairpin siRNA, as described in any of the embodiments above. In yet other embodiments, the strand is a multiplex siRNA molecule, as described in any of the embodiments above.

[0012] The present invention also provides a composition comprising a DNA molecule comprising a promoter operably linked to a sequence encoding at least one strand of a siRNA molecule, as described in any of the embodiments above. In other embodiments, the present invention also provides a composition comprising a DNA molecule comprising a first promoter operably linked to a first sequence encoding a first strand of a double stranded siRNA molecule and a second promoter operably linked to a second sequence encoding a second strand of the double stranded siRNA molecule. In other embodiments, the present invention provides a composition comprising a DNA molecule comprising a first promoter operably linked to a first sequence encoding a first hairpin siRNA molecule as described in any of the embodiments above and a second promoter operably linked to a second sequence encoding a second hairpin siRNA molecule as described in any of the embodiments above. In other embodiments, the present invention provides a composition comprising a DNA molecule comprising a first promoter

operably linked to a first sequence encoding a multiplex siRNA molecule as described in any of the embodiments above and a second promoter operably linked to a second sequence encoding a multiplex siRNA molecule as described in any of the embodiments above.

[0013] The present invention also provides a method for synthesizing siRNA molecules in vitro, comprising combining in vitro a DNA molecule comprising a sequence encoding at least one strand of a siRNA molecule operably linked to a promoter as described in any of the embodiments above, and an in vitro transcription system suitable for transcribing RNA from the promoter, such that the at least one encoded strand of a siRNA is transcribed. In some embodiments, the in vitro transcription system comprises a bacteriophage RNA polymerase; in other embodiments, the in vitro transcription system comprises prokaryotic RNA polymerase, and in other embodiments, the in vitro transcription system comprises a eukaryotic polymerase.

[0014] The present invention also provides a method for synthesizing siRNA molecules in vivo, comprising transfecting a cell with a DNA molecule comprising a sequence encoding at least one strand of an siRNA molecule as described in any of the embodiments above operably linked to a promoter, wherein the promoter can be expressed in the cell, such that the at least one encoded strand of a siRNA is transcribed. In some embodiments, the cell is an animal cell; in other embodiments, the cell is a mammalian cell.

[0015] The present invention also provides a method for inhibiting the function of a target RNA molecule, comprising combining a hairpin siRNA molecule as described in any of the embodiments above and a system comprising the target RNA and in which the function of the target RNA molecule can be inhibited by a siRNA molecule, thereby inhibiting the function of the target RNA molecule.

[0016] The present invention also provides a method for inhibiting the function of a target RNA molecule, comprising transfecting a cell with a hairpin siRNA molecule as described in any of the embodiments above, where the cell comprises a target RNA molecule to which either the first region or the third region of the hairpin siRNA molecule is complementary, thereby inhibiting the function of the target RNA molecule. In some embodiments, the cell is a mammalian cell, and in other embodiments, the cell is a human cell. In some other embodiments, the cell is in an organism.

[0017] The present invention also provides a method for inhibiting gene expression, comprising transfecting a cell with a hairpin siRNA molecule as described in any of the embodiments above, where the cell comprises a gene encoding a target RNA molecule to which either the first region or the third region of the hairpin siRNA molecule is complementary, thereby inhibiting the expression of the gene. In some embodiments, the cell is a mammalian cell, and in other embodiments, the cell is a human cell. In some other embodiments, the cell is in an organism.

[0018] The present invention also provides a method for inhibiting gene expression, comprising expressing a hairpin siRNA molecule in a cell, wherein the cell is transfected with a DNA molecule comprising a promoter operably linked to a sequence encoding the hairpin siRNA molecule as described in any of the embodiments above, and wherein the cell comprises a gene encoding a target RNA molecule to which either the first region or the third region of the hairpin

siRNA molecule is complementary, thereby inhibiting expression of the gene. In some embodiments, the cell is a mammalian cell, and in other embodiments, the cell is a human cell. In some other embodiments, the cell is in an organism.

[0019] The present invention also provides a method for inhibiting gene expression, comprising transfecting a cell with a DNA molecule comprising a promoter operably linked to a sequence encoding a hairpin siRNA molecule as described in any of the embodiments above, wherein the cell comprises a gene encoding a target RNA molecule to which either the first region or the third region of the hairpin siRNA molecule is complementary, and expressing the hairpin siRNA molecule in the cell, thereby inhibiting the expression of the gene. In some embodiments, the cell is a mammalian cell, and in other embodiments, the cell is a human cell. In some other embodiments, the cell is in an organism.

[0020] The present invention also provides a method for inhibiting gene expression, comprising expressing a first strand and a second strand of a ds siRNA molecule in a cell, wherein the cell is transfected with a DNA molecule comprising a first promoter operably linked to a first sequence encoding the first strand of a ds siRNA molecule and a second promoter operably linked to a second sequence encoding the second strand of the ds siRNA molecule, and wherein the cell comprises a gene encoding a target RNA molecule to which either the first strand or the second strand of the ds siRNA molecule is complementary, thereby inhibiting expression of the gene. In some embodiments, the cell is a mammalian cell, and in other embodiments, the cell is a human cell. In some other embodiments, the cell is in an organism.

[0021] The present invention also provides a method for inhibiting gene expression, comprising transfecting a cell with a DNA molecule comprising a first promoter operably linked to a first sequence encoding a first strand of a ds siRNA molecule and a second a promoter operably linked to a second sequence encoding a second strand of the ds siRNA molecule, wherein the cell comprises a gene encoding a target RNA molecule to which either the first strand or the second strand of the ds siRNA molecule is complementary, and expressing the encoded first strand and the encoded second strand of the ds siRNA molecule in the cell, thereby inhibiting the expression of the gene. In some embodiments, the cell is a mammalian cell, and in other embodiments, the cell is a human cell. In some other embodiments, the cell is in an organism.

[0093] The terms "promoter element," "promoter," or "promoter sequence" as used herein, refer to a DNA sequence that is located at the 5' end (i.e. precedes) the protein coding region of a DNA polymer. The location of most promoters known in nature precedes the transcribed region. The promoter functions as a switch, activating the expression of a gene. If the gene is activated, it is said to be transcribed, or participating in transcription. Transcription involves the synthesis of mRNA from the gene. The promoter, therefore, serves as a transcriptional regulatory element and also provides a site for initiation of transcription of the gene into mRNA.

[0094] Promoters may be tissue specific or cell specific. The term "tissue specific" as it applies to a promoter refers to a promoter that is capable of directing selective expression of a nucleotide sequence of interest to a specific type of tissue (e.g., seeds) in the relative absence of expression of the same nucleotide sequence of interest in a different type of tissue (e.g., leaves). Tissue specificity of a promoter may be evaluated by, for example, operably linking a reporter gene to

the promoter sequence to generate a reporter construct, introducing the reporter construct into the genome of a plant such that the reporter construct is integrated into every tissue of the resulting transgenic plant, and detecting the expression of the reporter gene (e.g., detecting mRNA, protein, or the activity of a protein encoded by the reporter gene) in different tissues of the transgenic plant. The detection of a greater level of expression of the reporter gene in one or more tissues relative to the level of expression of the reporter gene in other tissues shows that the promoter is specific for the tissues in which greater levels of expression are detected. The term "cell type specific" as applied to a promoter refers to a promoter that is capable of directing selective expression of a nucleotide sequence of interest in a specific type of cell in the relative absence of expression of the same nucleotide sequence of interest in a different type of cell within the same tissue. The term "cell type specific" when applied to a promoter also means a promoter capable of promoting selective expression of a nucleotide sequence of interest in a region within a single tissue. Cell type specificity of a promoter may be assessed using methods well known in the art, e.g., immunohistochemical staining. Briefly, tissue sections are embedded in paraffin, and paraffin sections are reacted with a primary antibody that is specific for the polypeptide product encoded by the nucleotide sequence of interest whose expression is controlled by the promoter. A labeled (e.g., peroxidase conjugated) secondary antibody that is specific for the primary antibody is allowed to bind to the sectioned tissue and specific binding detected (e.g., with avidin/biotin) by microscopy.

[0095] Promoters may be constitutive or regulatable. The term "constitutive" when made in reference to a promoter means that the promoter is capable of directing transcription of an operably linked nucleic acid sequence in the absence of a stimulus (e.g., heat shock, chemicals, light, etc.). Typically, constitutive promoters are capable of directing expression of a transgene in substantially any cell and any tissue. Exemplary constitutive plant promoters include, but are not limited to SD Cauliflower Mosaic Virus (CaMV SD; see e.g., U.S. Pat. No. 5,352,605, incorporated herein by reference), mannopine synthase, octopine synthase (ocs), superpromoter (see e.g., WO 95/14098), and ubi3 (see e.g., Garbarino and Belknap, Plant Mol. Biol. 24:119-127 (1994)) promoters. Such promoters have been used successfully to direct the expression of heterologous nucleic acid sequences in transformed plant tissue.

[0096] In contrast, a "regulatable" or "inducible" promoter is one which is capable of directing a level of transcription of an operably linked nuclei acid sequence in the presence of a stimulus (e.g., heat shock, chemicals, light, etc.) which is different from the level of transcription of the operably linked nucleic acid sequence in the absence of the stimulus.

[0097] The enhancer and/or promoter may be "endogenous" or "exogenous" or "heterologous." An "endogenous" enhancer or promoter is one that is naturally linked with a given gene in the genome. An "exogenous" or "heterologous" enhancer or promoter is one that is placed in juxtaposition to a gene by means of genetic manipulation (i.e., molecular biological techniques) such that transcription of the gene is directed by the linked enhancer or promoter. For example, an endogenous promoter in operable combination with a first gene can be isolated, removed, and placed in operable combination with a second gene, thereby making it a "heterologous promoter" in operable combination with the second gene. A variety of such combinations are contemplated (e.g., the first and second genes can be from the same species, or from different species.

[0140] The use of siRNAs to inhibit gene expression in host cells, and in particular in mammalian cells, is a promising new approach for the analysis of gene function. However, current methods suffer from several disadvantages, which include an expensive chemical synthesis of siRNA and the requirement that cells be induced to take up exogenous nucleic acids, which is a short-term treatment and is very difficult to achieve in some cultured cell types, and which does not permit long-term expression of the siRNA in cells or use of siRNA in tissues, organs, and whole organisms. It had also not been demonstrated that siRNA could effectively be expressed from recombinant DNA constructs to suppress expression of a target gene.

[0141] During the development of the present invention, the possibility of synthesizing siRNAs within host cells, and in particular within mammalian cells, using an expression vector was explored as a means to facilitate the delivery of siRNAs. A siRNA expression vector would facilitate transfection experiments in cell culture, as well as allow the use of transgenic or viral delivery systems. As a first step, siRNA designs better suited to expression vectors were evaluated; one such design is a hairpin RNA, in which both strands of a siRNA duplex are included within a single RNA molecule and the strands connected by a loop at one end. To facilitate testing different siRNA designs, a method was developed for an inexpensive and rapid procedure for siRNA synthesis; this method comprises the use of RNA transcription by bacteriophage RNA polymerases. In particular, the T7 in vitro transcription from oligonucleotide templates (Milligan, J. F. et al. (1987) Nucleic Acids Res 15, 8783-98) was used. This method was used to synthesize both conventional (or double stranded, or ds) and hairpin siRNAs, as well as mutant versions of these molecules. Gene inhibition was demonstrated by in vitro transcribed ds siRNAs and hairpin siRNAs using transfection into mouse P19 cells (mouse P19 cells are a model system for neuronal differentiation).

[0142] For synthesis of siRNAs in cells, an objective was to express short RNAs with defined ends in cells.

[0143] Transcriptional termination by RNA polymerase III is known to occur at runs of four consecutive T residues in the DNA template (Tazi, J. et al. (1993) Mol Cell Biol 13, 1641-50; and Booth, B. L., Jr. & Pugh, B. F. (1997) J Biol Chem 272, 984-91), providing one mechanism to end a siRNA transcript at a specific sequence. In addition, previous studies have demonstrated that the RNA polymerase III based expression vectors could be used for the synthesis of short RNA molecules in mammalian cells (Noonberg, S. B. et al. (1994) Nucleic Acids Res 22, 2830-6; and Good, P. D. et al. (1997) Gene Ther 4, 45-54). While most genes transcribed by RNA polymerase III require cis-acting regulatory elements within their transcribed regions, the regulatory elements for the U6 small nuclear RNA gene are contained in a discrete promoter located 5' to the U6 transcript (Reddy, R. (1988) J Biol Chem 263, 15980-4).

[0144] Using an expression vector with a mouse U6 promoter, as described in more detail below and in Examples 1, 5 and 6, it was discovered that both hairpin siRNAs and pairs of single-stranded siRNAs expressed in cells (which are contemplated to form duplex or ds siRNA) can inhibit gene expression. Inhibition by hairpin siRNAs expressed from the U6 promoter was discovered to be more effective than the other methods tested, including the transfection of in vitro synthesized ds siRNA. Moreover, inhibition by hairpin siRNAs is sequence-specific, as a

two base mismatch between an in vitro synthesized hairpin siRNA and its target abolished inhibition, and even a single base mismatch in one hairpin strand allowed differential inhibition of sense and antisense target strands.

See also paragraphs 238-245, and 265-267. turner et al have provided ample guidance for the selection and utilization of various promoters and in various configurations where it is clearly taught that one in the art can provide promoters in various configurations with not more than routine experimentation to optimize expression for a selected tissue type, cell type , or organism, for example.

Brummelkamp et al and Paddison et al have also taught that siRNA an shRNA compounds can be effectively expressed from vectors.

Hertzel el et al have taught the use of weak promoters in the expression of genes in adipose cells. It is taught that weak promoters are useful in the study of low-expressing genes. The study was performed using fluorescent reporters (see especially page 1085, for example).

Clearly one in the art would include the siRNA compounds of the prior art et al in the vectors taught by Nilsen et al. Nilsen et al clearly describe their vectors for the general purpose of identifying RNA affector molecules of which siRNA would clearly be a member. Nilsen et al have taught that the vectors provide for an efficient method of detecting effective RNA affector molecules through the use of reporter target RNA fusions. One intent on detecting effective affector molecules to inhibit low-expressing genes would look to the use of weak promoters as shown by Hertzel et al. The limitation of claim 162 where the polypeptide is lethal is considered an obvious variation for the following reasons. First, it is noted that the claim does not limit the polypeptide lethality to be due to the reporter aspect or the target RNA aspect of the fusion. Since the vector

of Nilsen et al also comprises a second reporter it would have been a fine tool to detect the inhibition of lethal nucleic acids in a cell since the second reporter would provide evidence that the surviving cells contained the vector with the test affector RNA targeting a lethal target gene, for example. Furthermore, Nilsen et al teach that a reporter molecule can be directly or indirectly detectable. Clearly a reporter that is lethal would provide for a detection of cells inhibiting the fusion polypeptide and those that do not. Nilsen et al has taught the instant methods where the difference is the use of siRNA which was not known at the time of Nilsen et al. the prior art has shown that siRNA and other RNA interfering compounds can be expressed from vectors as taught by Nilsen where various promoters are taught and various promoter orientations have also been taught. one in the art would select cell types to screen for RNA interfering compounds that would relate to a cell type. One in the art, for example would surly choose neuronal cells to screen for inhibitors of genes involved in neural disease, for example. The instant invention appears to amount to the utilization of a new compound [albeit known before the instant invention] in a known method.

The invention as a whole would therefore have been *prima facie* obvious to one in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R. McGarry whose telephone number is (571) 272-0761. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, J. Douglas Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sean R McGarry
Primary Examiner
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